## REMARKS/ARGUMENTS

Petition is hereby made under the provisions of 37 CFR 1.136(a) for an extension of three months of the period for response to the Office Action. Our cheque in respect of the prescribed fees is enclosed.

The Examiner reiterated objection to the drawings made in paragraph 7 of Paper No. 14. Formal drawings are enclosed which, it is submitted, remedy the defects noted in the PTO-948 attached to paper No. 14.

The withdrawal of the following rejections is gratefully acknowledged:

- the rejection of claim 2 under 35 USC 112, second paragraph, as being indefinite.

- the rejection of claims 7 and 8 under 35 USC 112, first paragraph, as being non-enabled, with regard to the deposit issue.

- the rejection of claims 1, 5 to 7, 9 and 10 under 35 USC 102(a) as being anticipated by Loosmore et al (USP 6,391,313)

- the rejection of claims 1, 5, 6, 9 and 10 under 35 USC 102(b) as being anticipated by Sasaki et al (WO 96/34960). It is noted, however, that the Examiner has entered a new rejection of claims 1, 2, 5, 6, 9 and 10 under 35 USC 102(b) in the Office Action based on this same prior art.

- the rejection of claims 7 and 8 under 35 USC 112, first paragraph, as being non-enabled with regard to scope.

The Examiner maintained rejection of claim 9 under 35 USC 112, second paragraph, as being indefinite. In this regard, claim 9 has been amended to refer to a C-terminal half of the about kDa protein, with the reference to "an approximately" being deleted. It is submitted that claim 9 can no longer be

considered to be indefinite and hence the rejection thereof under 35 USC 112, second paragraph, should be withdrawn.

The Examiner maintained rejection of claims 1, 2, 5, 6, 9 and 10 with respect to part (c) of claim 1 under 35 USC 102(e), as being anticipated by Sasaki et al USP 5,808,024 ('024)

The Office Action indicates that the Examiner again is providing a copy of Figure 6 of Sasaki et al '024 with ATG and GGG areas boxed and highlighted in colours. Regrettably, it would appear that this illustration again was not received or, if received, misplaced.

The Examiner is correct that claim 1(a) does not structurally define or identify by sequence number the "another strain of *Moraxella catarrhalis*". However, the claim does identify certain specific characteristics of the nucleotide sequence encoding an about 200 kDa outer membrane protein of such strain. The strains are clearly other than strains 4223, Q8 and LES-1, which are identified in parts (a) and (b) of claim 1. Part (c) of claim 1 has been amended to clarify this matter.

The Examiner comment that part 1(c) does not exclude any specific strain of *M. catarrhalis* is not clear, since nucleotide sequences encoding 200 kDa protein of *M. catarrhalis* strain and not having the recited characteristics are not within the scope of the claims and the "another strain of *Moraxella catarrhalis*".

According to part (c) of claim 1, the nucleotide sequence has several characteristics:

1. It must encode an about 200 kDa outer membrane protein of a strain of *Moraxella* other than strains 4223, Q8 and LES-1.

2. It must have a tract of consecutive G nucleotides which is 3 or a multiple thereof in length.

3. It must have an ATG start codon about 80 to 90 bp upstream of the tract.

4. The tract of consecutive G nucleotides must be located between amino acids 25 and 35 encoded by the nucleotide sequence.

The Examiner asserts that the term "amino acids 25 and 35 encoded by the nucleotide sequence" is ambiguous (it is noted that no rejection of claim 1 under 35 USC 112, second paragraph, has been made on this ground). The Examiner indicates that there is no indication where exactly the residue numbering should start from and where exactly amino acids 25 and 35 are in an amino acid sequence.

It is submitted that it is self evident that, in accordance with normal convention, amino acid number 1 is the first amino acid which is coded by the nucleotide sequence, in this case the recited ATG start codon. The amino acids 25 and 35 are the twenty-fifth and thirty-fifth amino acids of the about 200 kDa outer membrane protein of *M. catarrhalis* which is encoded by the defined nucleotide sequence.

The Examiner is correct that the GGG tract is part of the nucleotide sequence. To avoid any suggestion that the G tract is in the amino acid sequence, (an impossibility), claim 1 has been amended to recite that the tract is located in a portion of the nucleotide sequence which encodes a portion of the outer membrane protein between amino acids 25 and 35.

In his comments, the Examiner was troubled by the term "about" to describe the location of G tract "about" 80 to 90 bp upstream of the tract and applies a strained interpretation in discussing the rejection. The term "about" has been deleted from claim 1.

The Examiner is correct that the nucleotide sequence is required to encode an outer membrane protein of a strain of *M. catarrhalis* (excluding, of

course, strains 4223, Q8 and LES-1, which are claimed elsewhere in the claim) and has to have a GGG or GGGGGG etc tract and an ATG codon 80 to 90 bp upstream of the tract. In addition, as discussed above, the tract is required to be located in a portion of the nucleotide sequence which encodes a portion of the 200 kDa protein between amino acids 25 and 35.

In considering the cited prior art of Figure 6 of Sasaki et al '024, it is necessary to consider what the reference actually discloses. Figure 6A is the nucleotide sequence of the fragment of nucleic acid between a Sal I and an NcoI restriction sites. The Figure is described in the reference as:

> "Fig. 6 shows the nucleotide sequence (SEQ ID No:1) of the gene having an open reading frame of the about 200 kDa outer membrane protein of *M. catarrhalis*".

The Figure does not show the opening reading frame or any encoded amino acid sequence. The reference makes no attempt to identify the start codon of the open reading frame, vaguely indicating that somewhere in the Figure there is an open reading frame encoding an about 200 kDa outer membrane protein of a strain of *M. catarrhalis*.

The Examiner indicates that the prior art nucleotide sequence structurally meets the nucleotide sequence claimed in part (c) of claim 1. The Examiner takes the view that the nucleotide sequence disclosed in Figure 6 encodes an outer membrane protein of a strain of *Moraxella catarrhalis*. However, the portion of the nucleotide sequence which encodes an outer membrane protein is not identified in the Figure. In addition, the strain of *M. catarrhalis* from which the nucleotide sequence of Figure 6 was derived is strain 4223, which is specifically excluded from part (c) of claim 1.

The Examiner indicates that the sequence present in Figure 6 of Sasaki et al '024 has:

(a) one GGG tract about 102 bp upstream of the tract (The Examiner equates about 102 bp to "about 80 to 90 bp"),

(b) a second GGG tract about 86 bp upstream of the tract (which the Examiner equates as "about 80 to 90 bp) and an ATG codon structure at a second portion of the sequence; and

(c) a third GGG tract about 74 bp upstream of the tract (which the Examiner equates to "about 80 bp") and an ATG codon structure at a third portion of the sequence.

The Examiner indicates that a copy of Figure 6 is enclosed with the Office Action with the sequence in question highlighted. However, as noted above, applicants are not in possession of this Figure.

Provided twice.

In any event, as also noted previously, the term "about" has been deleted from claim 1(c) with respect to the 80 to 90 bp range. The Examiner appears to have simply selected GGG tracts and ATG codons he has located in the sequence of Figure 6 of Sasaki et al '024. There is no evidence provided by Figure 6 or elsewhere in Sasaki et al to suggest that <u>any</u> of the ATG codons identified by the Examiner is a start condon of a reading frame of the nucleotide sequence encoding a 200 kDa outer membrane protein of a strain of *Moraxella catarrhalis*.

NO still exists.

It is noted that Sasaki et al subsequently identified the start codon as a GTG codon (see WO 96/34960 cited by the Examiner).

For these various reasons, it is submitted claims 1, 2, 6, 9 and 10 are not anticipated by Sasaki et al '024 and hence the rejection thereof under 35 USC 102(e) as being anticipated by the cited prior art should be withdrawn.

The Examiner maintained rejection of claims 1, 2, 5, 6, 9 and 10 under 35 USC 112, first paragraph, as being non-enabled with respect to the scope.

As has already explained, part (c) of claim 1 does not include strains 4223, Q8 and LES-1, for the simple reason that these strains are encompassed by parts 1(a) and 1(b) of the claim and reference is made to another *Moraxella catarrhalis* strain, i.e. a strain other than already claimed in the claims. In any event, also as noted above, claim 1(c) now recites a strain other than 4223, Q8 and LES-1.

The Examiner is correct that the nucleotide sequence claimed in claim 1(c) is not structurally defined, in terms of providing a specific sequence of nucleotide identified by SEQ ID No. However, as already explained in discussing the prior art rejection, the characteristics of the nucleotide sequence are provided and it is a routine matter for a person skilled in the art to determine if any specific nucleotide sequence of *Moraxella catarrhalis* strain which encodes an about 200 kDa outer membrane protein of the strain possesses the characteristics recited.

No undue experimentation is required, contrary to the suggestion of the Examiner. A person skilled in the art possessed of a nucleotide sequence derived from a strain of *Moraxella catarrhalis* need only:

1. Determine if the sequence encodes an about 200 kDa outer membrane protein of the strain;

2. Determine the sequence of nucleotides in the nucleic acid molecule; and

3. Examine the nucleotide sequence to determine whether the criteria recited in claim 1(c) are met.

It is not seen where any undue experimentation is involved.

Table 1A lists a large number of strains of *Moraxella catarrhalis*, the anatomical origin of the strain, the source of the strain and the level of expression of the 200 kDa protein in such strains. Table 1B lists a large number of strains of *Moraxella catarrhalis* and provides the results of bactericidal assays against these

strains using recombinant M56 200 kDa protein (see preparation in Example 7), protein from strains 4223 and LES-1 and the recombinant C-terminal half of 200 kDa protein from strain 4223 (see preparation in Example 15). The assay itself is described in Example 11.

The applicants have shown that the number of G nucleotides in the G tract had a regulatory function in the expression of the 200 kDa protein. The examination of 25 strains of *M. catarrhalis*, as presented in Table 5, strongly suggests that the number of G nucleotides in the G tract controls the expression of the 200 kDa gene in *M. catarrhalis* strains. Thus, a strain of *M. catarrhalis* strongly expressing the 200 kDa protein is a strain that reasonably would be expected to have a nucleotide sequence having the characteristics of claim 1(c).

The Examiner comments on the results of Table 5 stating:

> "Table 5 does not exclude the three (+++) 200 kDa protein-producing strain of *M. catarrhalis* to be strains 4223, Q8 and LES-1, nor does it identify these strains to be strains other than 4223, Q8 and LES-1".

As described in Example 3, the data presented in Table 5 was generated by identifying a series of strains expressing a 200 kDa gene by immunoblot analysis and the 5' end of these 200 kDa genes was PCR amplified and sequenced. A person skilled in the art is well able to conduct exactly these experiments.

As seen in Table 5, 15 strains showing strongly expressing (+++) the 200 kDa protein possessed a G tract which is three or a multiple of three G's and possesses an ATG start codon. 3 strains showing low levels of expression (+) of the 200 kDa protein had 10 Gs and a GTG start codon while five strains showing no level of expression (-) of 200 kDa protein had 7 and 8 Gs in the tract.

It is not necessary to identify the specific strains as being 4223, Q8 or LES or any other strain. What is shown by Table 5 that the number of Gs in the tract affects the expression of 200 kDa protein in strains of *M. catarrhalis*.

Having regard to the above, since the applicants have identified, by experimentation, the characteristics required for the nucleotide sequences defined in claim 1(c), they were in possession of the nucleotide sequences recited therein. As already indicated, it is within the routine skill of the art, once provided with the criteria of claim 1 (c) and the experimentation set forth in applicants specification, to determine whether any specific nucleotide sequence which encodes an about 200 kDa outer membrane protein of a strain of *Moraxella catarrhalis* meets the requirements of part 1(c) of claim 1.

The Examiner asserts, without any justification:

> "…. the observation obtained from the genetic analysis regarding one of *M. catarrhalis* that expresses the 200 kDa protein cannot be extrapolated to every other 200 kDa protein-expressing strain of *M. catarrhalis*."

Applicants provide evidence to the contrary and, as noted in the specification, similar enhancement of transcriptional control are found for other bacterial genes, such as *N. gonorrhoae Pilc* gene (see ref. 32).

Having regard to the above, it is submitted that claims 1, 2, 5, 6, 9 and 10 are fully enabled with respect to part (c) of claim 1 and hence the rejection thereof under 35 USC 112, first paragraph, should be withdrawn.

The Examiner rejected claims 1, 2, 5, 6, 9 and 10 under the judicially-created doctrine of obviousness-type double patenting over claims 1, 3 to 7, 9 and 10 of US Patent No. 6,448,386.

The Examiner expresses the view that SEQ ID No. 2 of USP 6,448,386, a vector and host cell comprising the same anticipate the claim identified. The Examiner relies on columns 41 to 46 (which contain the sequence listing for SEQ ID No: 2), Figure 6 (which is the same Figure 6 as that contained in the Sasaki et al '082 patent discussed above) containing the sequence of SEQ ID No:2 and lines 54 to 61 of column 6 (which contain the description of Figure 6).

As already fully described above, Figure 6 (SEQ ID No:2) discloses only a nucleotide sequence. There is no start codon identified and hence it is unknown why the Examiner refers to amino acids 25 and 35 of a 200 kDa protein encoded by the nucleotide sequence and an ATG start codon. No start codon is identified and neither is an open reading frame. Col. 6, lines 54 to 61 discloses that an GTG is the start codon and that the donwstream ATG is a putative start codon only.

US Patent No. 6,448,386 does not "anticipate" claims 1, 2, 5, 6, 9 and 10 and hence the rejection thereof under the judicially-created doctrine of obviousness-type double patenting over claims 1, 3 to 7, 9 and 10 of US Patent No. 6,448,386, should be withdrawn.

The Examiner rejected claims 1, 2, 5, 6, 9 and 10 under the judicially-created doctrine of obviousness-type double patenting over claims 5 to 13 of US Patent No. 5,808,024. The disclosure of USP '024 has been fully discussed above. As already stated, the Figure 6 is a nucleotide sequence. No start codon is identified and neither is the open reading frame.

Accordingly, it is submitted that claims 1, 2, 5, 9 and 10 do not constitute an obviousness-type double patenting of claims 5 to 13 of US Patent No. 5,808,024. The rejection of claims 1, 2, 5, 6, 9 and 10 under the judicially-created doctrine of obviousness-type double patenting over claims 5 to 13 of US Patent No. 5,808,024, therefore, should be withdrawn.

The Examiner rejected claims 1, 2, 5, 6, 9 and 13 under 35 USC 102(b) as being anticipated by Sasaki et al (WO 96/34960).

In the prior Office Action, the Examiner had rejected claims 1, 5, 6, 9 and 10 as being anticipated by this prior art. Arguments were presented in response to the rejection. In the latest Office Action, the Examiner states that he has withdrawn the rejection of claims 1, 5, 6, 9 and 10 under 35 USC 102(b) as being anticipated by Sasaki et al (WO 96/34960). Yet, in the same Office Action, the

Examiner now has rejected claims 1, 2, 5, 6, 9 and 10 as being anticipated by Sasaki et al (WO 96/34960). Having withdrawn the rejection in view of the arguments provided, it is not known why the Examiner at the same time makes the same rejection of the same claims (with the exception of claim 2) based on the same prior art.

As was explained in response to the prior Office Action, the Sasaki et al WO reference and its contents are fully described in the specification. The comments made above with respect to the Sasaki US Patent No. 5,808,024 apply equally here.

The Examiner refers to a copy of Figure 6 of Sasaki et al WO with certain boxing and highlighting. No such material accompanied the Office Action.

In common with USP 5,808,024, WO 96/34960 has only a nucleotide sequence in Figure 6 with no ATG or other start codon or open reading frame identified.

Having regard to the above, it is submitted that claims 1, 2, 5, 6, 9 and 10 are not anticipated by Sasaki et al WO 96/34960 and hence the rejection thereof under 35 USC 102(e) as being anticipated by such prior art, should be withdrawn.

The Examiner rejected claims 1, 2, 5, 6, 9 and 10 as being anticipated by Sasaki et al US Patent No. 6,448,386 ('386).

The content of Sasaki et al '386 has been discussed above with respect to the double patenting rejection based thereon. SEQ ID No: 2, on which the Examiner relies, is a nucleotide sequence only with no identification of a start codon or an open reading frame col. 6, lines 54 to 61 does not disclose that an ATG is the start codon but rather that GTG is the start codon and the ATG is merely a putative start codon (see sequence 1 and encoded amino acid sequence indicated therein).

Accordingly, it is submitted that claims 1, 2, 5, 6, 9 and 10 are not anticipated by Sasaki et al ('386) and hence the rejection thereof under 35 USC102(e) as being anticipated by the cited prior art, should be withdrawn.

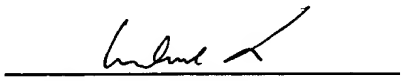
The Examiner rejected claims 1, 2, 5, 6, 9 and 10 under 35 USC 102(e) as being anticipated by Sasaki et al US Patent No. 6,440,425 ('425). This rejection would appear to be repetitious of the prior rejection, in that the same description text is used to support the same argument.

These disclosures have been fully discussed above. There are no new points that have been made by the Examiner with respect to the cited prior art. Having regard to the points already made, it is submitted that claims 1, 2, 5, 6, 9 and 10 are not anticipated by Sasaki et al '425 and hence the rejection thereof under 35 USC 102(e) as being anticipated by this prior art, should be withdrawn.

The Examiner indicated that claims 7 and 8 were objected to as being dependent from a base rejected claim. These claims have been rewritten in independent form. It is submitted that claims 7 and 8 now are in an allowable form.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,



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